glial, neuronal and endothelial markers demonstrating pluripotency of differentiation potential. These findings point towards an essential role of CD133/Musashi-1+ cells in glioma biology making these cells a potential target for future therapies. On the other hand, stem cells are currently evaluated as potential carriers of anti-glioma therapies. Therefore, the second aim of our studies was to assess intracerebral distribution patterns of mesenchymal stroma cells (MSC) after local versus systemic application. Human MSC (hMSC) were isolated from bone marrow biopsies carried out for haematological indications. U373-GFP gliomas were generated by orthotopic implantation. After local application of hMSC, migration of hMSC towards the tumor was observed. In a second setting, intravenously administered MSC transfected with a RFP/Tie-2 promotor gene showed extensive tropism to the glioma. RFP expression indicated integration of MSC into the intratumoral vasculature. Therefore, MSC might be valuable candidates as carriers for an anti-tumor, especially an anti-vascular gene therapy. Altogether, stem cells might play roles in the "cause" as well as in the "cure" of glioma.

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S49. TARGETED DELIVERY OF CHEMOTHERAPY USING MICROENCAPSULATED CELLS FOR GDEPT

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Some of the most potent cytotoxic drugs, e.g. ifosfamide, are hampered in their effectiveness in certain cancers due to severe side effects in elder patients. A way to circumvent this problem is to employ gene directed enzyme prodrug therapy by delivering a second site of drug activation at the tumor site. This concept was developed using ifosfamide as the prodrug and the metabolising cytochrome P450 subenzyme CYP2B1 for conversion. The gene was transfected in 293 cells. To protect the genetically modified cells from the host immune system and, conversely, to protect the host from the allogenic cells, those were microencapsulated in sodium cellulose (diameter $\approx$ 0.8 mm). In an experimental setting, the microcapsules containing CYP2B1 expressing cells were directly injected in pre-established human pancreatic adenocarcinomas on nude mice. After treatment with low-dose ifosfamide, 20% CR was achieved. Identical results were obtained in a syngenic rat pancreatic carcinoma model. Further, this experimental approach has very successfully been applied to experimental peritoneal carcinomatosis as well as naturally occurring breast carcinomas in dogs. For clinical use, a feasibility study in pigs demonstrated the safety of agiographic intra-arterial placement into a pancreatic artery. After completion of IRB and registration with authorities, a clinical phase I/II study in patients with inoperable pancreatic adenocarcinoma was performed. The concept proved to be safe. 2/14 patients demonstrated a partial remission, the reminder was stable. Mean OS was 44 weeks, one year survival 32%.

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S50. DEVELOPING STRATEGIES FOR TUMOR VACCINATION

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Vaccination against cancer has had a variable history, with claims of success often fading into disappointment. The reasons for this include poor vaccine design, inadequate understanding of the nature of the immune response, and a lack of objective measures to evaluate performance. The characterization of tumor-associated antigens (TAAs) recognized by human T lymphocytes in a MHC-restricted fashion has opened new possibilities for specific vaccine approaches to the treatment of human cancers. Recent findings include vaccine formulation, relevant knowledge concerning mechanisms of induction of effective immunity from preclinical models, and translation into clinical trials. We now have novel vaccine strategies to activate specific attack on tumor cells and we understand more about activation and regulation of immunity against cancer (co-stimulation versus co-inhibition, regulatory T cells). We also have modern assays using surrogate markers (MHC multimer analysis, IFN-γ Elispot assay) to correlate with clinical effects. Although early clinical vaccine trials based on synthetic peptides, proteins, 'naked' DNA, tumor-RNA, dendritic cells, and recombinant vaccinia viruses indicate that vaccines can induce immune responses and tumor regression in some cancer patients, careful study design and use of standardized clinical and immunological criteria are needed. Basic principles of tumor vaccination and clinical trials will be discussed.

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S51. MOLECULAR STAGING OF THYROID CANCERS AND ASSOCIATED FAMILIAL SYNDROMES – CONSEQUENCES FOR SCREENING AND THERAPY

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Disseminated tumor cells in tissue, blood or bone marrow samples of patients with thyroid carcinoma are detectable by PCR assays by using different molecular tumor markers. The aim of our study was to correlate the results of molecular staging with the patients' follow-up.

Patients and Methods: Eighty-seven tumor, 43 blood and 14 bone marrow samples of patients with thyroid carcinomas were obtained during surgery and subjected to Cytokeratin 20 (CK20) and PreproGastrin-releasing peptide (PreproGRP) PCR systems.

Results: An expression of CK20 transcripts was detected in all of the medullary thyroid carcinomas (MTC), 63% of follicular thyroid carcinomas (FTC), 43% of papillary (PTC) and 17% of anaplastic (ATC) carcinomas . In FTC and PTC an expression of CK20 was seen in 54% in primary tumors and in 42% in soft tissue or lymph node recurrence. 75% of the patients with CK20-positive FTC were disease-free at follow-up compared to none of the patients with CK20-negative FTC. PreproGRP was found in 100% of MTC tissue samples. Overall, disseminated tumor cells of CK20-positive carcinomas were detected in 33% of the blood samples. In MTC,